

REMARKSStatus of the Claims

Claims 1-14, 16-20, 25-31, 33, 34, 56, 57, 67, 68, 92, 93, 95, and 115-121 are pending and were rejected. No amendments have been made to these claims. New claims 122-125, which depend from claim 1, have been added. Support for the new claims is found throughout the specification, for example at page 77, last paragraph, through page 78. The new claims add no new matter. Entry of the amendment is respectfully requested.

The grounds for rejection have been carefully considered. Reconsideration of the rejection in view of the following remarks is respectfully requested.

Rejections under 35 U.S.C. § 103

Claims 1-11, 13, 16-20, 25-31, 34, 67, 68, 92, 93, 95, and 115-121 were rejected as allegedly obvious based on Kaye in view of Wu, et al. (US 6,221,677). According to the examiner, Kaye allegedly discloses a microdevice having certain features within the scope of claim 1. Furthermore, as alleged by the Examiner:

Kaye et al. also teach using the microdevice to test the ability of library elements or compounds to modulate activity in biological systems, including cells, enzymes, receptors (See page 19, line 1-5). However, Kaye et al. do not disclose the features of having a binding partner, e.g. antibody, capable of binding to a moiety to be manipulated and with magnetic material thereon.

Wu et al. teach immobilizing binding partner capable of being manipulated on the beads having magnetic materials (see Figure 4). The binding of the analyte can be separated or isolated by magnetic force. Supra.

Therefore, it would have been obvious to one ordinary skill in the art at the time the invention was made to have provided Kaye et al. with the binding partner, such as antibody, immobilized on a magnetic beads in order to improve efficiency of separation or isolation of the modulated target molecules.

Respectfully, the Examiner has misinterpreted what Kaye discloses. Here is the passage from Kaye on which the Examiner relies to support the above statements, beginning with the two paragraphs preceding the passage that the Examiner singled:

Furthermore, the combinatorial compound library may comprise any convenient number of individual members, for example tens to hundreds to thousands to millions etc., of suitable compounds, for example, peptides, peptoids, other oligomeric compounds (cyclic or linear), and template-based molecules, for example benzodiazepines, hydantoins, biaryls, polycyclic compounds (e.g., naphthalenes, phenothiazines, acridines, steroids etc.), carbohydrate and amino acid derivatives, dihydropyridines, benzhydryls, and heterocycles (e.g., triazines, indoles, etc.). The numbers quoted and the types of compounds listed are illustrative but not limiting.

The compound library preferably comprises chemical compounds of low molecular weight and potential therapeutic agents. Such compounds are for example of less than about 1000 daltons, such as less than 800, 900, or 400 daltons.

Combinatorial Libraries are intended for testing in a variety of assays. The purpose of any assay is to test the ability of library elements or compounds to modulate activity in a test system of interest. Particularly preferred, but in no way limiting, are biological assays, biological systems and biologicals of interest including high throughput screens. Convenient biologicals of interest include proteins such as enzymes, receptors, signaling systems, reporter genes and the like. Suitable test systems will be apparent to the scientist of ordinary skill. Any convenient number of library compounds may be tested in the biological assay.

Kaye, pg. 18, line 13 to pg. 19, line 8.

The most significant feature of that passage from Kaye is the fact that it makes *absolutely no mention of a 'microdevice'*. The passage merely describes a Combinatorial Library, which may be synthesized with devices that Kaye discloses, and ways such a library of compounds could be tested for any type of activity. The combinatorial libraries are, according to Kaye, a separate aspect of Kaye's invention. ("Chemical libraries synthesized on a plurality of coded microparticles as hereinbefore defined are novel and represent further and independent aspects of this invention." Kaye, pg. 19, lines 10-12.)

The first step in the Graham analysis is determining the scope and content of the prior art. The Examiner asserts that this passage teaches using the microdevice "to test the ability of library

elements or compounds to modulate activity in biological systems.” However, that is not what this passage from Kaye describes. Because the very basis for the Examiner’s rejection was not derived from the reference, and the Examiner has misinterpreted the scope and content of the primary reference that was relied upon, the analysis is not based on correct analysis of the prior art and cannot therefore reach a correct conclusion of obviousness: this rejection is improper and should be withdrawn.

In addition, it is unclear how the Examiner’s conclusion is even based in the alleged disclosures of the references. The Examiner says it would have been obvious “to have provided Kaye et al. with the binding partner, such as antibody, immobilized on a magnetic beads in order to improve efficiency of separation or isolation of the modulated target molecules.” However, the only ‘modulated target molecules’ in Kaye appear to be those discussed in the passage about screening a combinatorial library. Those ‘modulated’ target molecules are not being separated or isolated; they are merely involved in the characterization of the activity or lack thereof of a library of compounds. Kaye does not disclose or suggests that those ‘modulated target molecules’ are being manipulated in any way *or* that they are associated with the device Kaye discloses. Thus the Examiner’s conclusion relies upon a use of the device from Kaye that is neither disclosed nor suggested by Kaye: Kaye does not disclose or suggest use of its devices to manipulate those ‘modulated target molecules’. This manipulation of those target molecules appears to be conceived only in hindsight, based on the applicant’s disclosure. Such a hindsight reconstruction of the invention is improper and cannot support an obviousness rejection. Accordingly, the rejection should be withdrawn.

Moreover, the Examiner relied upon Kaye as the primary reference for this rejection, and modified it to incorporate features allegedly disclosed by Wu. However, the combination made by the Examiner changes the principle of operation of the primary reference: it introduces magnetic material solely for the purpose of manipulating the particles, while the primary reference does not provide any means in the particle for such manipulation. Such a modification of the device changes the principle of operation that Kaye discloses, which is improper. MPEP 2143.01(IV): “If the proposed modification or combination of the prior art would change the principle of operation of the

prior art invention being modified, then the teachings of the references are not sufficient to render the claims *prima facie* obvious. *In re Ratti*, 270 F.2d 810, 123 USPQ 349 (CCPA 1959)."

Accordingly, this combination cannot be properly relied upon to establish a *prima facie* obviousness case. For this additional reason, the rejection based on Kaye in view of Wu has been overcome and should be withdrawn.

Dependent Claims

The foregoing demonstrates that no *prima facie* case for an obviousness rejection of claim 1 has been established. The Examiner relied upon other passages to address certain limitations of the dependent claims, and some of those are discussed separately to show that these additional limitations are not disclosed by the references, so the dependent claims are patentable even if claim 1 were rendered obvious.

The Examiner alleges that claims 13 and 28-31 are obvious because "Kaye et al. also teach using electromagnetic materials for facilitation of the binding by physical force, such as magnetic interaction (see page 15, line 15-17)."

Here is the passage from Kaye that is relied upon for that rejection: "A further embodiment of this application comprises subparticles which are derived from a non-porous, rigid, inert material such as silicate (glass) into which has been deposited, during or after production, but before association with the solid support, a suitable number of individual materials which can be altered by application of an external non-chemical stimulus, for example electromagnetic radiation." Kaye, page 15, 12-17.

Thus the passage allegedly disclosing "electromagnetic materials..." in fact mentions only "electromagnetic radiation." It does not disclose or suggest use of electromagnetic materials in a microdevice. Furthermore, claim 31 requires a plurality of elements that facilitate or enable manipulation; and the Examiner's comments do not indicate multiple elements are disclosed. The rejection of claims 13 and 28-31 therefore has NO basis in the reference and should be withdrawn.

With respect to claim 26, the Examiner merely says that “the antibodies taught by Wu et al. can be manipulated, e.g. binding to the analyte. Surpa [sic].” While it is not clear just what that means, claim 26 relates to a binding partner that is a cell, cellular organelle, or virus. Neither Kaye nor Wu discloses or suggests a cell, cellular organelle or virus that is associated with a microdevice. Since neither reference discloses or suggests such features, the references do not disclose or suggest all limitations of this claim, so they cannot provide a *prima facie* basis for a rejection. Accordingly, this rejection should be withdrawn.

Claims 12 and 14 were rejected based on Kaye and Wu, further in view of Zhou et al., US 6,355,491. According to the Examiner, Zhou et al “teach different materials, such as glass, silicon dioxide, aluminum, silicon dioxide or nickel alloy layers...” The Examiner cites passages in Zhou, though, that have *nothing* to do with a device that resembles the claimed microdevices. The fact that other materials are known in the art is irrelevant to an obviousness analysis: they must be known to be suitable for the present use in order for their use to be *prima facie* obvious. The passages of Zhou to which the Examiner refers relate to the devices depicted in Zhou Figure 1 and Zhou Figure 10; neither of those could fairly be compared to the claimed microdevices.

The relevant standard from the MPEP refers to substituting a material that is recognized in the art to be suitable for the same purpose. “MPEP 2144.07 Art Recognized Suitability for an Intended Purpose.” The Examiner has not shown that Zhou’s device is similar to the one claimed: as illustrated in its Figures, Zhou’s device is a relatively large, complex device having “arrays of individually addressable micro-electromagnetic units...” (Zhou Abstr.) Thus the cited reference has no relevance to the microdevice of the claims, and a list of materials that may be useful for making a device such as the one described in Zhou does not disclose or suggest that those materials are ‘recognized in the art’ as suitable for use in the claimed microdevice. This rejection is improper and should be withdrawn.

Moreover, claim 14 is drawn to a particular CoTaZr alloy that is not disclosed or suggested in any of the cited references. This claim has a limitation that has not been identified in any cited

reference; accordingly, the references cannot establish a *prima facie* basis for obviousness rejection of this claim. This rejection should be withdrawn.

New claims 122-125 describe a patterned magnetic material, and requires the patterned material to be either nickel or a CoTaZr alloy. None of the references describe a patterned magnetic material having these characteristics. The patterned magnetic material provides an unexpected advantage, because they produce microdevices that orient parallel to each other when in a magnetic field, as illustrated in Figures 7-9, and such controlled orientation makes the microdevices easier to identify and observe. Accordingly, these claims are believed to avoid all previous rejections and to be patentable over all cited references.

Summary

Kaye does not teach a device that is adapted to be manipulated by magnetic forces or one that is adapted to use a binding partner according to claim 1 to carry or manipulate a moiety. The Examiner's proposal to modify the Kaye device to introduce two such new functional features dramatically alters the basic principle of Kaye's device, which is a labeled support for constructing and characterizing a combinatorial library of synthetic molecules. (See Kaye's title and abstract and the passage of Kaye cited above.) That dramatic alteration of the primary reference clearly violates the MPEP's prohibition against modifying a primary reference's disclosure in a way that alters the basic operating principle of the primary reference. MPEP 2143.01(VI): "If the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims *prima facie* obvious. *In re Ratti*, 270 F.2d 810, 123 USPQ 349 (CCPA 1959)." Such an obviousness analysis is improper. Therefore, no *prima facie* case for a rejection has been provided, and the rejections that rely on modifying Kaye to incorporate features from Wu have been overcome and should be withdrawn.

In addition, the analysis is improper because it is entirely based on hindsight. Evidence of that is clear: the Examiner asserts that Kaye describes use of a microdevice to test a library, but the

passage cited for that assertion does not refer to a microdevice at all, only to ways a combinatorial library could be used. The Examiner asserted that another passage in Kaye disclosed embodiments relevant to claims 13 and 28-31, because it allegedly disclosed an 'electromagnetic material,' which the Examiner seemed to equate to the magnetic material of claim 13 and the element in claims 28-31. Again, the reference does not disclose what the Examiner refers to: it does not describe any sort of magnetic material at all. *The only possible way to interpret either of these passages as relating to the invention as claimed is with a strong hindsight bias*, having the claimed device in mind rather than the content of the reference. Federal Circuit case law repeatedly cautions that an obviousness rejection based on hindsight is improper; and the *Graham* analysis requires an accurate determination of the scope and content of the prior art, which is missing in this case. This rejection is based on hindsight, as is proven by the Examiner's misinterpretation of the content of the references. This rejection is thus improper and should be withdrawn.

Conclusion

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. **471842000500**. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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